

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

Status of Previously Applied Actions

The Examiner has entered Applicants' substitute specification and declaration filed 3 January 2000, as well as Applicants' substitute drawings.

The Examiner has withdrawn the rejection of claims 1-9 and 21-27 under 35 U.S.C. §112, first paragraph.

The Examiner has withdrawn the rejection of claims 1-9 and 21-27 under 35 U.S.C. §112, second paragraph.

The Examiner has withdrawn the rejection of claims 1-9 and 22-24 under 35 U.S.C. §103(a) in view of Karube, *et al.*, and Sleight, *et al.*

The Examiner has withdrawn the rejection of claims 21 and 25 under 35 U.S.C. §103(a) in view of Karube, *et al.*, Sleight, *et al.*, and Miller, *et al.*

Current Grounds of Rejection:

The Examiner has maintained in part the rejection of claims 21, 22, 25, and 26 under 35 U.S.C. §112, first paragraph, asserting that the claims contain subject matter which was not described in the specification.

The Examiner has provisionally rejected claims 1-9 and 21-27 under the judicially created doctrine of obviousness-type double patenting, asserting that the claims are unpatentable over claims 1-18 of co-pending Application No. 09/183,566.

The Examiner has rejected claims 1-9, 22-23 and 27 under 35 U.S.C. §102(b) asserting that the claims are anticipated by Karube, *et al.*, in light of Sleight, *et al.*.

The Examiner has rejected claims 21 and 25 under 35 U.S.C. §103(a) asserting that the claims are unpatentable over Karube, *et al.*, in light of Sleight, *et al.*, and further in view of Garcia Vescovi, *et al.*

These rejections are traversed for reasons discussed below.

Addressing the Examiner's Rejections

1. Rejection of Claims 21, 22, 25 and 26 under 35 U.S.C. §112, First Paragraph

The Examiner has maintained in part the rejection of claims 21, 22, 25, and 26 under 35 U.S.C. §112, first paragraph, asserting that the claims contain subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, has possession of the claimed invention, *i.e.*, a lack of adequate written description.

The remaining issue under 35 U.S.C. §112, first paragraph, relates to the language recited in claim 22 “sheltered in a genetically engineered bacterial cell.” In view of the Examiner’s recitation of this language as the remaining grounds of rejection, the only claim that remains rejected under 35 U.S.C. §112, first paragraph, is claim 22 because it is the only claim reciting this limitation. Accordingly, the rejections of claims 21, 25, and 26 appear to have been withdrawn in view of Applicants arguments in the response dated 28 December 1999.

The Examiner asserts the following in the remaining rejection of claim 22:

“While the specification (page 13, lines 28-29) teaches examples of living cells which can be genetically altered for use as biodetectors. The specification does not appear to teach a biodetector within a genetically engineered cell.” (Office action, page 3, lines 9-12.)

The Examiner’s position is unclear to the Applicants. The subject matter in question is clearly described in the specification as originally filed. First, there is an entire section of the specification describing “Entities Sheltering Biodetectors,” page 13 to page 14. Second, the specification specifically recites the following:

“The biological components of the biodetector may be contained in or otherwise may be attached to living or non-living entities that stabilize essential interactions.” Specification, page 13, lines 20-21.

The specification goes on to recite the following:

“Most typically, the biodetector entity is a living cell which is genetically engineered to comprise all required components. Living entities include, but are not limited to, prokaryotes, eukaryotes, viruses, retroviruses, vectors, plasmids, phage, transformed eukaryotic cells, such as lymphocytes, macrophages, established cell lines. Most typically, **the entity sheltering (is) a genetically engineered bacterial cell, as *E. coli*.**” Specification, page 13, lines 24-28. These recitations appear to the Applicants to directly contradict the Examiner assertion that “(t)he specification does not appear to teach a biodetector within a genetically engineered cell.”

Compliance with the written description requirement is a question of fact. It is a fact in this case that the specification explicitly recites and describes the limitation of presented in claim

22. Under the “PTO Revised Examiner Guidelines on Written Description Requirement,” the Examiner is required to do the following when making a rejection based on written description:

“(1) identify the claim limitation at issue; and

(2) establish a *prima facie* case by providing reasons why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed.” (Section III “Complete Patentability Determination Under All Statutory Requirements and Clearly Communicate Findings, Conclusions, and Their Bases.”)

The Applicants submit that the Examiner has failed to establish a *prima facie* case. The Examiner has not provided reasons why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed. Accordingly, in view of the above arguments the Applicants submit that claim 22 complies with the requirements of 35 U.S.C. §112, first paragraph, and that the rejection of the claim should be withdrawn.

2. Obviousness-Type Double Patenting

The Examiner has provisionally rejected claims 1-9 and 21-27 under the judicially created doctrine of obviousness-type double patenting, asserting that the claims are unpatentable over claims 1-18 of co-pending Application No. 09/183,566.

Applicants request that evaluation of this rejection be held in abeyance until Applicants and the USPTO agree upon allowable subject matter.

3. Rejections Under 35 U.S.C. §102(b)

The Examiner has rejected claims 1-9, 22-23 and 27 under 35 U.S.C. §102(b) asserting that the claims are anticipated by Karube, *et al.*, in light of Sleight, *et al.*

In support of this rejection the Examiner states the following:

“Karube, *et al.*, anticipates claims 1-9, 22-23 and 27. Sleight, *et al.*, is not used as a secondary reference in combination with Karube, *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Karube, *et al.*, because Sleight, *et al.*, teaches the signal transduction pathways whereby an extracellular signal molecule binds to a

native receptor on the cell surface which then results in the generation of an intracellular signal.” Office action, dated 5 June 2000, page 6, lines 17-25.

The Examiner goes on to state:

“Karube disclose biosensors, however, the reference does not specifically recite the extracellular ligand-specific moiety and an intracellular signal transforming domain.” Office action, dated 5 June 2000, page 7, lines 11-13.

Accordingly, the Examiner has acknowledge that the reference of Karube, *et al.*, does not teach all of the elements of the claim. To anticipate a claim, a single source must contain all of the elements of the claim. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 USPQ 81, 90 (Fed. Cir. 1986). *Atlas Powder Co. v. E. I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 USPQ 409, 411 (Fed. Cir. 1984).

The Examiner goes on to make up for the deficiencies of Karube, *et al.*, by invoking the teachings of Sleight, *et al.* (Office action, dated 5 June 2000, page 7, lines 14-19). This is inappropriate because missing elements may not be supplied by the knowledge of one skilled in the art or the disclosure of another reference. *Structural Rubber Prods. Co. v. Park Rubber Co.*, 749 F.2d 707, 716, 223 USPQ 1264, 1271 (Fed. Cir. 1984). Moreover, the single source must disclose all of the claimed elements “arranged as in the claims.” *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ 2d 1913, 1920 (Fed. Cir. 1989).

Anticipation under §102 can be found only when the reference discloses exactly what is claimed. Where there are differences between the reference disclosure and the claim, the rejection must be based on §103 which takes differences into account. *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 780, 227 USPQ 773, 777 (Fed. Cir. 1985). Applicants have previously argued the Examiner’s rejection of claims 1-9 and 22-24 under 35 U.S.C. §103(a) in view of Karube, *et al.*, and Sleight, *et al.* In view of Applicants’ arguments, the Examiner has withdrawn this basis of rejection (Office action, dated 5 June 2000, page 3, lines 17-19).

In view of the above arguments, the Applicants submit that rejection of the claims under 35 U.S.C. §102(b) is inappropriate and should be withdrawn.

4. Rejections Under 35 U.S.C. §103

The Examiner has rejected claims 21 and 25 under 35 U.S.C. §103(a) asserting that the claims are unpatentable over Karube, *et al.*, in light of Sleigh, *et al.* (as applied to claims 1-9, 22-23 and 27), and further in view of Garcia Vescovi, *et al.*

As discussed in Applicants' response (dated 28 December 1999) to the Office action dated 2 July 1999, neither the primary (Karube, *et al.*) nor secondary (Sleigh, *et al.*) references cited by the Examiner provide any motivation for the making of a biodetector comprising (a) a signal converting element, having an extracellular ligand-specific moiety and an intracellular signal transforming domain, where the extracellular ligand-specific moiety selectively recognizes the selected substance, which recognition activates said intracellular signal transforming domain; (b) a transducer, where the transducer has an inactive and an active form which are distinct from each other, and where the activated intracellular signal transforming domain converts the inactive form of the transducer into the active form of the transducer; and (c) a responsive element, where the responsive element is activated by the active form of the transducer, resulting in a detectable signal.

The Examiner, as discussed in Applicants' response dated 28 December 1999, did not provide any evidence of a motivation to combine the cited references along the lines of the present invention. Accordingly, the Applicants submitted that the rejection of Claims 1-9, 22-24 and 27 in view of Karube, *et al.*, and Sleigh, *et al.*, was improper and should be withdrawn. As noted above, in view of Applicants' arguments, the Examiner has withdrawn this basis of rejection under 35 U.S.C. §103(a) (Office action, dated 5 June 2000, page 3, lines 17-19).

It is now the Examiner's opinion that claims 21 and 25 are rendered obvious in view of Karube, *et al.*, in light of Sleigh, *et al.* (as applied to claims 1-9, 22-23 and 27), and further in view of Garcia Vescovi, *et al.* First, Karube, *et al.*, in light of Sleigh, *et al.*, does not anticipate the present invention for the reasons presented above. Second, the Examiner has withdrawn the previous rejection of claims 1-9 and 22-24 under 35 U.S.C. §103(a) in view of Karube, *et al.*, and Sleigh, *et al.*. Accordingly, the Applicants submit that there is no basis for the current rejection of dependent claims 21 and 25 in view of the fact that the independent claims appear to be free of the art. The dependent claims 21 and 25 distinguish over the prior art at least in view of their dependencies on the independent claims.

However, in this rejection of claims 21 and 25 under 35 U.S.C. §103(a) the Examiner asserts the following:

"The teachings of Karube, *et al.*, in light of Sleight, *et al.*, were set forth above. The references, however, differ in not teaching (the) PhoQ 2-component system as the signal transducer." Office action, dated 5 June 2000, page 8, lines 5-7.

The Examiner goes on to assert the following:

"Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the biodetector of Karube, *et al.*, with the signal transduction system of Garcia vescovi, *et al.* One of ordinary skill in the art would have been motivated to do this in order to detect the presence or absence of magnesium in an environment." Office action, dated 5 June 2000, page 8, lines 15-20.

As discussed above, Karube, *et al.*, does not teach the elements of the present invention and as discussed in Applicants' previous response (dated 28 December 1999) Sleight, *et al.*, does not make up for the shortcomings of Karube, *et al.* The observation in Garcia Vescovi, *et al.*, that magnesium acts as an extracellular signal mediated via the two-component PhoP/PhoQ system does nothing to make up for the short-comings of Karube, *et al.*, and Sleight, *et al.* The teachings of Garcia Vescovi, *et al.*, do not suggest adapting a PhoP/PhoQ two-component system to be part of a biosensor or biodetector as claimed in Claims 21 and 25.

The Examiner relies on the use of prohibited reconstructive hindsight to formulate the present rejection. The Examiner has picked and chosen among the references based on the teachings of the applicant. There is nothing in the cited references to provide a nexus between the different teachings of the cited prior art concerning the biosensor or biodetector as claimed in Claims 21 and 25.

Even if, *in arguendo*, the elements of the present invention were taught in the prior art, the Federal Circuit in *Symbol Technologies, Inc. v. Opticon, Inc.*, 935 F.2d 1569, 19 USPQ2d 1241 (Fed. Cir. 1991) stated the following:

"We do not pick and chose among the individual elements of assorted prior art references to recreate the claimed invention, but rather, we look for some teaching or suggestion in the references to support their use in the particular claimed combination."

Prior to the teachings of the present specification, there was no indication in the prior art that one of ordinary skill in the art would choose to create a biodetector for the detection of a selected substance as described in independent claim 1.

As stated above, absent a motivation to combine the cited references along the lines of the claimed invention, the Examiner is using prohibited hindsight to piece together the prior art to defeat patentability. In *Grain Processing Corp. v. American Maize-Products Corp.*, 840 F.2d 902, 5 USPQ2d 1788 (Fed. Cir. 1988), the court stated:

"Care must be taken to avoid hindsight reconstruction by using the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the results of the claims in suit."

Accordingly, the Applicants submit that the rejection of Claims 21 and 25 in view of Karube, *et al.*, Sleigh, *et al.*, and Miller, *et al.*, is improper and should be withdrawn.

CONCLUSION

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

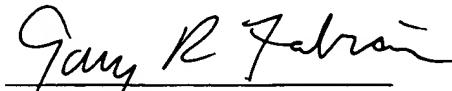
Please direct all further communications in this application to:

Charles Sholtz, Ph.D., Esq.
Director, Intellectual Property
Xenogen Corporation
860 Atlantic Avenue
Alameda, CA 94501
Phone: 510-291-6135 / Fax: 510-291-6134

Respectfully submitted,

Date: 6 Nov 2000

By:



Gary R. Fabian, Ph.D.
Registration No. 33,875
Agent for Applicants